WEST Search History

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DATE: Thursday, January 15, 2004

Hide?	Set Name	Query	Hit Count
	DB=PGPB; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L3	human adj5 acyltransferase	20
	DB=USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L2	human adj5 acyltransferase	54
☐	L1	human adj5 acytransferase	0

END OF SEARCH HISTORY

```
=> file .nash

=> s human and acyltransferase and (gene or clon? or dna or cdna or rna or nucleic acid)
L1          852 FILE MEDLINE
L2          553 FILE CAPLUS
L3          520 FILE SCISEARCH
L4          101 FILE LIFESCI
L5          481 FILE BIOSIS
L6         1389 FILE EMBASE

TOTAL FOR ALL FILES
L7         3896 HUMAN AND ACYLTRANSFERASE AND (GENE OR CLON? OR DNA OR CDNA OR
                RNA OR NUCLEIC ACID)

=> s human (5w) acyltransferase and (gene or clon? or dna or cdna or rna or nucleic acid)
TOTAL FOR ALL FILES
L14         484 HUMAN (5W) ACYLTRANSFERASE AND (GENE OR CLON? OR DNA OR CDNA OR
                RNA OR NUCLEIC ACID)

=> s l7 not 2002-2004/py

TOTAL FOR ALL FILES
L21        3040 L7 NOT 2002-2004/PY

=> s l21 and glycerol
TOTAL FOR ALL FILES
L28          77 L21 AND GLYCEROL

=> dup rem l28
PROCESSING COMPLETED FOR L28
L29          46 DUP REM L28 (31 DUPLICATES REMOVED)

=> d ibib abs 1-46

L29  ANSWER 1 OF 46  CAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2002:43345  CAPLUS
DOCUMENT NUMBER:          136:319709
TITLE:                    Transcriptional profiling reveals global defects in
                          energy metabolism, lipoprotein, and bile acid
                          synthesis and transport with reversal by leptin
                          treatment in Ob/ob mouse liver
AUTHOR(S):                Liang, Chien-Ping; Tall, Alan R.
CORPORATE SOURCE:         Division of Molecular Medicine, Department of
                          Medicine, Columbia University, New York, NY, 10032,
                          USA
SOURCE:                   Journal of Biological Chemistry (2001), 276(52),
                          49066-49076
                          CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER:                American Society for Biochemistry and Molecular
                          Biology
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Leptin, a hormone secreted by adipose tissue, has been shown to have a
     major influence on hepatic lipid and lipoprotein metab. To characterize
     changes in lipid and lipoprotein gene expression in mouse liver,
     suppression subtractive hybridization and cDNA microarray anal.
     were used to identify mRNAs differentially expressed after leptin
     treatment of ob/ob mice. Ob/ob mice showed a profound decrease in mRNAs
     encoding genes controlling bile acid synthesis and transport as
     well as a variety of apolipoprotein genes and hepatic lipase
     with reversal upon leptin administration, suggesting that leptin
     coordinately regulates high d. lipoprotein and bile salt metab. Leptin
     administration also resulted in decreased expression of genes
     involved in fatty acid and cholesterol synthesis, glycolysis,
     gluconeogenesis, and urea synthesis, and increased expression of
     genes mediating fatty acid oxidn., ATP synthesis, and oxidant
     defenses. The changes in mRNA expression are consistent with a switch in
     energy metab. from glucose utilization and fatty acid synthesis to fatty
     acid oxidn. and increased respiration. The latter changes may produce
     oxidant stress, explaining the unexpected finding that leptin induces a
```

battery of **genes** involved in antioxidant defenses. Expression cluster anal. revealed responses of several sets of **genes** that were kinetically linked. Thus, the mRNA levels of **genes** involved in fatty acid and cholesterol synthesis are rapidly (<1 h) repressed by leptin administration, in assocn. with an acute decrease in plasma insulin levels and decreased sterol regulator element-binding protein-1 expression. In contrast, **genes** participating in fatty acid oxidn. and ketogenesis were induced more slowly (24 h), following an increase in expression of their common regulatory factor, peroxisome proliferator-activated receptor .alpha.. However, the regulation of **genes** involved in high d. lipoprotein and bile salt metab. shows complex kinetics and is likely to be mediated by novel transcription factors.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 2 OF 46 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 1

ACCESSION NUMBER: 2002:190572 BIOSIS
DOCUMENT NUMBER: PREV200200190572
TITLE: Mitochondrial **glycerol** phosphate **acyltransferase** directs the incorporation of exogenous fatty acids into triacylglycerol.
AUTHOR(S): Igal, R. Ariel; Wang, Shuli; Gonzalez-Baro, Maria; Coleman, Rosalind A. [Reprint author]
CORPORATE SOURCE: Depts. of Nutrition and Pediatrics, University of North Carolina, CB No. 7400, Chapel Hill, NC, 27599-7400, USA rcoleman@unc.edu
SOURCE: Journal of Biological Chemistry, (November 9, 2001) Vol. 276, No. 45, pp. 42205-42212. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Mar 2002
Last Updated on STN: 13 Mar 2002

AB The mitochondrial isoform of **glycerol**-3-phosphate **acyltransferase** (GPAT), the first step in glycerolipid synthesis, is up-regulated by insulin and by high carbohydrate feeding via SREBP-1c, suggesting that it plays a role in triacylglycerol synthesis. To test this hypothesis, we overexpressed mitochondrial GPAT in Chinese hamster ovary (CHO) cells. When GPAT was overexpressed 3.8-fold, triacylglycerol mass was 2.7-fold higher than in control cells. After incubation with trace (14C)oleate (apprx3 muM), control cells incorporated 4.7-fold more label into phospholipid than triacylglycerol, but GPAT-overexpressing cells incorporated equal amounts of label into phospholipid and triacylglycerol. In GPAT-overexpressing cells, the incorporation of label into phospholipid, particularly phosphatidylcholine, decreased 30%, despite normal growth rate and phospholipid content, suggesting that exogenous oleate was directed primarily toward triacylglycerol synthesis. Transiently transfected HEK293 cells that expressed a 4.4-fold increase in GPAT activity incorporated 9.7-fold more (14C)oleate into triacylglycerol compared with control cells, showing that the effect of GPAT overexpression was similar in two different cell types that had been transfected by different methods. When the stable, GPAT-overexpressing CHO cells were incubated with 100 muM oleate to stimulate triacylglycerol synthesis, they incorporated 1.9-fold more fatty acid into triacylglycerol than did the control cells. Confocal microscopy of CHO and HEK293 cells transfected with the GPAT-FLAG construct showed that GPAT was located correctly in mitochondria and was not present elsewhere in the cell. These studies indicate that overexpressed mitochondrial GPAT directs incorporation of exogenous fatty acid into triacylglycerol rather than phospholipid and imply that (a) mitochondrial GPAT and lysophosphatidic acid **acyltransferase** produce a separate pool of lysophosphatidic acid and phosphatidic acid that must be transported to the endoplasmic reticulum where the terminal enzymes of triacylglycerol synthesis are located, and (b) this pool remains relatively separate from the pool of lysophosphatidic acid and phosphatidic acid that contributes to the synthesis of the major phospholipid species.

L29 ANSWER 3 OF 46 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:887210 CAPLUS

DOCUMENT NUMBER: 136:148924
TITLE: Identification of novel **genes** differentially expressed in omental fat of obese subjects and obese type 2 diabetic patients
AUTHOR(S): Corominola, Helena; Conner, Laura J.; Beavers, Lisa S.; Gadski, Robert A.; Johnson, Dwayne; Caro, Jose F.; Rafaeloff-Phail, Ronit
CORPORATE SOURCE: Servei d'Endocrinologia, IDIBAPS-Institut d'Investigacions, Biomediques, August Pi i Sunyer Hospital Clinic, Barcelona, Spain
SOURCE: Diabetes (2001), 50(12), 2822-2830
CODEN: DIAEAZ; ISSN: 0012-1797
PUBLISHER: American Diabetes Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Obesity is assocd. with an increased risk for developing type 2 diabetes, insulin resistance, hypertension, dyslipidemia, cardiovascular disease, respiratory dysfunction, and certain forms of cancer. Insulin resistance in many type 2 diabetic patients is the result of increased visceral adiposity. To identify novel **genes** implicated in type 2 diabetes and/or obesity and to elucidate the mol. mechanisms underlying both diseases, the authors analyzed **gene** expression in omental fat from lean and obese nondiabetic subjects and obese type 2 diabetic patients using mRNA differential display and subtracted library techniques. After screening over 13,800 subtracted **cDNA clones** and 6,912 **cDNA** amplification products, the authors identified 2,078 **cDNAs** that showed potential differential expression in the omental fat of lean vs. obese nondiabetic subjects vs. obese type 2 diabetic patients. Data anal. showed that 70.7% of these **clones** corresponded to unknown **genes** (26.7% matched express sequence tags [ESTs]) and 29.3% corresponded to known **genes**. Reverse Northern and classic Northern analyses further confirmed that the expression of five of these **cDNA clones** was elevated in obese nondiabetic subjects and obese type 2 diabetic patients. Four candidate **genes** were further evaluated for tissue distribution, which showed expression primarily in adipose and skeletal muscle tissue, and chromosomal localization. The authors concluded that both mRNA differential display and subtracted **cDNA** libraries are powerful tools for identifying novel **genes** implicated in the pathogenesis of obesity and type 2 diabetes.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 4 OF 46 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2002044867 EMBASE
TITLE: Detection of tyrosinase mRNA in tumor tissue microdissections from classic Kaposi's sarcoma [2].
AUTHOR: Palmieri G.; Cossu A.; Lissia A.; Leoncini L.; Lazzi S.; Ascierto P.A.; Castello G.; Tanda F.
CORPORATE SOURCE: F. Tanda, Institute of Pathology, University of Sassari, Sassari, Italy. tandaf@ssmain.uniss.it
SOURCE: Annals of Oncology, (2001) 12/12 (1765-1766).
Refs: 5
ISSN: 0923-7534 CODEN: ANONE2
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
029 Clinical Biochemistry
LANGUAGE: English

L29 ANSWER 5 OF 46 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001441522 MEDLINE
DOCUMENT NUMBER: 21379957 PubMed ID: 11487472
TITLE: The structure and functions of **human** lysophosphatidic acid **acyltransferases**.
AUTHOR: Leung D W
CORPORATE SOURCE: Cell Therapeutics, Inc., Seattle, WA 98119, USA.. dleung@ctiseattle.com
SOURCE: FRONTIERS IN BIOSCIENCE, (2001 Aug 1) 6 D944-53. Ref: 34

Journal code: 9702166. ISSN: 1093-4715.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20020121
Entered Medline: 20011213

AB Lysophosphatidic acid (LPA) and phosphatidic acid (PA) are two phospholipids involved in signal transduction and in lipid biosynthesis in cells. LPA **acyltransferase** (LPAAT), also known as 1-acyl sn-**glycerol**-3-phosphate **acyltransferase** (1-AGPAT) (EC 2.3.1.51), catalyzes the conversion of LPA to PA. Two **human** isoforms of LPAAT, designated as LPAAT-alpha (AGPAT1) and LPAAT-beta (AGPAT2), have been extensively characterized. These two proteins contain extensive sequence similarities to microbial, plant and animal LPAAT sequences. LPAAT-alpha mRNA is uniformly expressed throughout most tissues with the highest level found in skeletal muscle; whereas LPAAT-beta is differentially expressed, with the highest level found in heart and liver, and negligible level in brain and placenta. The LPAAT-alpha **gene** is located on chromosome 6p21.3, an area within the class III region of the major hiscompatibility complex (MHC) and the LPAAT-beta **gene** is mapped to chromosome 9q34.3. Enhanced transcription of LPAAT-beta is suggested for neoplasm of the female genital tract. Additionally, ectopic LPAAT expression in certain cytokine-responsive cell lines can effect amplification of cellular signaling processes, such as those leading to enhancement of synthesis of tumor necrosis factor-alpha and interleukin-6 from cells following stimulation with interleukin-1beta; this suggests that the LPAAT **genes** represent candidates for affecting the development of certain cancers or inflammation-associated diseases.

L29 ANSWER 6 OF 46 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001216136 MEDLINE
DOCUMENT NUMBER: 21134310 PubMed ID: 11237722
TITLE: Etherphospholipid biosynthesis and dihydroxyactetone-phosphate **acyltransferase**: resolution of the genomic organization of the **human** gnpat **gene** and its use in the identification of novel mutations.
AUTHOR: Ofman R; Lajmir S; Wanders R J
CORPORATE SOURCE: Department of Clinical Chemistry and Pediatrics, Academic Medical Centre, Amsterdam, 1100 DE, The Netherlands.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (2001 Mar 2) 281 (3) 754-60.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF218223; GENBANK-AF218224; GENBANK-AF218225; GENBANK-AF218226; GENBANK-AF218227; GENBANK-AF218228; GENBANK-AF218229; GENBANK-AF218230; GENBANK-AF218231; GENBANK-AF218232; GENBANK-AF218233
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010425
Last Updated on STN: 20010425
Entered Medline: 20010419

AB Etherphospholipids are characterised by the occurrence of an alkyl- or alkenyl-group at the sn-1 position of the **glycerol** backbone. Peroxisomes play an essential role in the formation of etherphospholipids since the first two enzymes of the biosynthetic pathway are strictly peroxisomal. The function of plasmalogens is still an enigma but the recent identification of patients suffering from an isolated defect in either dihydroxyacetone phosphate **acyltransferase** (GNPAT) or alkyldihydroxyacetone phosphate synthase provides conclusive evidence that plasmalogens play an essential role for **human** survival and functioning. In this paper we report the complete genomic organisation of

the GNPAT **gene** coding for the peroxisomal dihydroxyacetone phosphate **acyltransferase**. The **gene** is located on chromosome 1q42.12-43. It spans approximately 28 kb and consists of 16 exons and 15 introns. This information was used to analyse the GNPAT **gene** in 12 patients with GNPAT deficiency. All patients analysed were found to have mutations in their GNPAT **gene**. Of the 9 different mutations found, 2 were missense mutations, 2 small deletions, 1 insertion and 3 mutations were within splice donor/acceptor-sites. Another mutation created an alternative splice donor-site causing the partial deletion of an exon. The data obtained provide conclusive evidence for the major role of GNPAT in etherphospholipid biosynthesis. Copyright 2001 Academic Press.

L29 ANSWER 7 OF 46 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:199675 BIOSIS
DOCUMENT NUMBER: PREV200100199675
TITLE: Lysophosphatidic acid, a novel lipid growth factor for **human** thyroid cells: Over-expression of the high-affinity receptor EDG4 in differentiated thyroid cancer.
AUTHOR(S): Schulte, Klaus-Martin [Reprint author]; Beyer, Andreas; Koehrer, Karl; Oberhaeuser, Simone; Roeher, Hans-Dietrich
CORPORATE SOURCE: Clinic for General Surgery and Trauma Surgery, Medizinische Einrichtungen, Heinrich-Heine University, Moorenstr. 5, 40225, Dusseldorf, Germany
SchulteKM@med.uni-duesseldorf.de
SOURCE: International Journal of Cancer, (15 April, 2001) Vol. 92, No. 2, pp. 249-256. print.
CODEN: IJCNAW. ISSN: 0020-7136.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Apr 2001
Last Updated on STN: 18 Feb 2002

AB Lysophosphatidic acid (LPA) is a small lipid mediator with pleiotropic biological activities, e.g., the regulation of cellular proliferation and various aspects of cellular physiology. Signal transduction is achieved by binding to 2 high-affinity receptors, EDG2 and EDG4, and a group of low-affinity receptors, EDG1-7, all belonging to the superfamily of G protein-coupled receptors. We examined the growth-regulatory effects of LPA in primary cultures of 8 goiters and 1 papillary thyroid cancer. We further assessed mRNA expression of high-affinity receptors EDG2 and EDG4 in 14 normal thyroids, 29 papillary thyroid cancers, 7 follicular thyroid cancers and 13 goiters by quantitative RT-PCR. We also identified mRNA expression of phospholipase A2 and LPA **acyltransferase** in fresh thyroid tissues derived from various sources. At concentrations of 10, 50 and 150 muM, LPA induced a 2-fold rise of proliferation ($p < 0.001$) and acted as strongly as thyrotropin. The combination of LPA and TSH produced significant synergistic effects compared with each substance alone ($p < 0.05$). Normal thyroid, goiter and papillary or follicular thyroid cancer expressed 2 high-affinity cognate LPA receptors, EDG2 and EDG4. EDG4 receptor mRNA expression was increased 3-fold in differentiated thyroid cancer ($p < 0.01$), both papillary ($p < 0.01$) and follicular ($p < 0.05$), compared to normal thyroid or goiter. Overall expression of EDG2 receptor was unchanged in malignancy; however, increased EDG2 expression in individual samples correlated with lymphonodular metastasis ($p = 0.01$). Thus, lipid mediators are a novel class of factors involved in the control of proliferation in the **human** thyroid. Altered mRNA expression of the high-affinity LPA receptor EDG4 suggests a role in the pathogenesis of differentiated thyroid cancer.

L29 ANSWER 8 OF 46 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001057402 EMBASE
TITLE: Overexpression of 1-acyl-**glycerol**-3-phosphate **acyltransferase**-.alpha. enhances lipid storage in cellular models of adipose tissue and skeletal muscle.
AUTHOR: Ruan H.; Pownall H.J.
CORPORATE SOURCE: Dr. H.J. Pownall, Department of Medicine, MS A-601, Baylor College of Medicine, 6565 Fannin St., Houston, TX 77030, United States. hpownall@bcm.tmc.edu
SOURCE: Diabetes, (2001) 50/2 (233-240).

Refs: 49
ISSN: 0012-1797 CODEN: DIAEAZ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Plasma nonesterified fatty acids (NEFA) at elevated concentrations antagonize insulin action and thus may play a critical role in the development of insulin resistance in type 2 diabetes. Plasma NEFA and glucose concentrations are regulated, in part, by their uptake into peripheral tissues. Cellular energy uptake can be increased by enhancing either energy transport or metabolism. The effects of overexpression of 1-acylglycerol-3-phosphate **acyltransferase** (AGAT)-.alpha., which catalyzes the second step in triglyceride formation from **glycerol** -3-phosphate, was studied in 3T3-L1 adipocytes and C2C12 myotubes. In myotubes, overexpression of AGAT-.alpha. did not affect total [(14)C]glucose uptake in the presence or absence of insulin, whereas insulin-stimulated [(14)C]glucose conversion to cellular lipids increased significantly (33%, P = 0.004) with a concomitant decrease (-30%, P = 0.005) in glycogen formation. [(3)H]oleic acid (OA) uptake in AGAT-overexpressing myotubes increased 34% (P = 0.027) upon insulin stimulation. AGAT-.alpha. overexpression in adipocytes increased basal (130%, P = 0.04) and insulin-stimulated (27%, P = 0.01) [(3)H]OA uptake, increased insulin-stimulated glucose uptake (56%, P = 0.04) and conversion to cellular lipids (85%, P = 0.007), and suppressed basal (-44%, P = 0.01) and isoproterenol-stimulated OA release (-45%, P = 0.03) but not **glycerol** release. Our data indicate that an increase in metabolic flow to triglyceride synthesis can inhibit NEFA release, increase NEFA uptake, and promote insulin-mediated glucose utilization in 3T3-L1 adipocytes. In myotubes, however, AGAT-.alpha. overexpression does not increase basal cellular energy uptake, but can enhance NEFA uptake and divert glucose from glycogen synthesis to lipogenesis upon insulin stimulation.

L29 ANSWER 9 OF 46 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:775265 CAPLUS
DOCUMENT NUMBER: 136:132090
TITLE: Investigation of differentially expressed **genes** during the development of mouse cerebellum
AUTHOR(S): Kagami, Yoshihiro; Furuichi, Teiichi
CORPORATE SOURCE: Laboratory for Molecular Neurogenesis, Brain Science Institute, RIKEN, Wako, 351-0198, Japan
SOURCE: Gene Expression Patterns (2001), 1(1), 39-59
CODEN: GEPEAD; ISSN: 1567-133X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Before the discovery of **DNA** microarray and **DNA** chip technol., the expression of only a small no. of **genes** could be analyzed at a time. Currently, such technol. allows us the simultaneous anal. of a large no. of **genes** to systematically monitor their expression patterns that may be assocd. with various biol. phenomena. We utilized the Affymetrix GeneChip Mu11K to analyze the **gene** expression profile in developing mouse cerebellum to assist in the understanding of the genetic basis of cerebellar development in mice. Our anal. showed 81.6% (10.321/12.654) of the **genes** represented on the GeneChip were expressed in the postnatal cerebellum, and among those, 8.7% (897/10.321) were differentially expressed with more than a two-fold change in their max. and min. expression levels during the developmental time course. Further anal. of the differentially expressed **genes** that were clustered in terms of their expression patterns and the function of their encoded products revealed an aspect of the genetic foundation that lies beneath the cellular events and neural network formation that takes place during the development of the mouse cerebellum.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 10 OF 46 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2000283580 MEDLINE
DOCUMENT NUMBER: 20283580 PubMed ID: 10747858
TITLE: A lecithin cholesterol **acyltransferase**-like **gene** mediates diacylglycerol esterification in yeast.
AUTHOR: Oelkers P; Tinkelenberg A; Erdeniz N; Cromley D; Billheimer J T; Sturley S L
CORPORATE SOURCE: Institute of Human Nutrition, Columbia University College of Physicians and Surgeons, New York, New York 10032, USA.
CONTRACT NUMBER: DK07715 (NIDDK)
HL07343 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 May 26) 275 (21) 15609-12.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000714
Last Updated on STN: 20000714
Entered Medline: 20000630

AB The terminal step in triglyceride biosynthesis is the esterification of diacylglycerol. To study this reaction in the model eukaryote, Saccharomyces cerevisiae, we investigated five candidate **genes** with sequence conservation to mammalian **acyltransferases**. Four of these **genes** are similar to the recently identified acyl-CoA diacylglycerol **acyltransferase** and, when deleted, resulted in little or no decrease in triglyceride synthesis as measured by incorporation of radiolabeled oleate or **glycerol**. By contrast, deletion of LRO1, a homolog of **human** lecithin cholesterol **acyltransferase**, resulted in a dramatic reduction in triglyceride synthesis, whereas overexpression of LRO1 yielded a significant increase in triglyceride production. In vitro microsomal assays determined that Lro1 mediated the esterification of diacylglycerol using phosphatidylcholine as the acyl donor. The residual triglyceride biosynthesis that persists in the LRO1 deletion strain is mainly acyl-CoA-dependent and mediated by a **gene** that is structurally distinct from the previously identified mammalian diacylglycerol **acyltransferase**. These mechanisms may also exist in mammalian cells.

L29 ANSWER 11 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:303476 SCISEARCH
THE GENUINE ARTICLE: 304AV
TITLE: Sterol regulation of **human** fatty acid synthase promoter I requires nuclear factor-Y- and Sp-1-binding sites
AUTHOR: Xiong S B; Chirala S S; Wakil S J (Reprint)
CORPORATE SOURCE: BAYLOR COLL MED, VERNA & MARRS MCLEAN DEPT BIOCHEM & MOL BIOL, 1 BAYLOR PLAZA, HOUSTON, TX 77030 (Reprint); BAYLOR COLL MED, VERNA & MARRS MCLEAN DEPT BIOCHEM & MOL BIOL, HOUSTON, TX 77030
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (11 APR 2000) Vol. 97, No. 8, pp. 3948-3953.
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 45
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB To understand cholesterol-mediated regulation of **human** fatty acid synthase promoter I, we tested various 5'-deletion constructs of promoter I-luciferase reporter **gene** constructs in HepG2 cells. The reporter **gene** constructs that contained only the Sp-1-binding site (nucleotides -82 to -74) and the two tandem sterol regulatory elements (SREs; nucleotides -63 to -46) did not respond to

cholesterol. Only the reporter **gene** constructs containing a nuclear factor-Y (NF-Y) sequence, the CCAAT sequence (nucleotides -90 to -86), an Sp-1 sequence, and the two tandem SREs responded to cholesterol. The NF-Y-binding site, therefore, is essential for cholesterol response. Mutating the SREs or the NF-Y site and inserting 4 bp between the Sp-1- and NF-Y-binding sites both resulted in a minimal cholesterol response of the reporter **genes**. Electrophoretic mobility-shift assays using anti-SRE-binding protein (SREBP) and anti-NF-Ya antibodies confirmed that these SREs and the NF-Y site bind the respective factors. We also identified a second Sp-1 site located between nucleotides -40 and -30 that can substitute for the mutated Sp-1 site located between nucleotides -82 and -74. The reporter **gene** expression of the wild-type promoter and the Sp-1 site (nucleotides -82 to -74) mutant promoter was similar when SREBP1a [the N-terminal domain of SREBP (amino acids 1-520)] was constitutively overexpressed, suggesting that Sp-1 recruits SREBP to the SREs. Under the same conditions, an NF-Y site mutation resulted in significant loss of reporter **gene** expression, suggesting that NF-Y is required to activate the cholesterol response.

L29 ANSWER 12 OF 46 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:154858 CAPLUS
DOCUMENT NUMBER: 132:277541
TITLE: Lipotoxic heart disease in obese rats: implications for **human** obesity
AUTHOR(S): Zhou, Yan-Ting; Grayburn, Paul; Karim, Asad; Shimabukuro, Michio; Higa, Moritake; Baetens, Dany; Orci, Lelio; Unger, Roger H.
CORPORATE SOURCE: Gifford Laboratories, Center for Diabetes Research, Department of Internal Medicine, University of Texas Southwestern Medical Center, Dallas, TX, 75390, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2000), 97(4), 1784-1789
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To det. the mechanism of the cardiac dilatation and reduced contractility of obese Zucker Diabetic Fatty rats, myocardial triacylglycerol (TG) was assayed chem. and morphol. TG was high because of underexpression of fatty acid oxidative enzymes and their transcription factor, peroxisome proliferator-activated receptor-.alpha.. Levels of ceramide, a mediator of apoptosis, were 2-3 times those of controls and inducible nitric oxide synthase levels were 4 times greater than normal. Myocardial **DNA** laddering, an index of apoptosis, reached 20 times the normal level. Troglitazone therapy lowered myocardial TG and ceramide and completely prevented **DNA** laddering and loss of cardiac function. In this paper, the authors conclude that cardiac dysfunction in obesity is caused by lipoapoptosis and is prevented by reducing cardiac lipids.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 13 OF 46 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001033578 EMBASE
TITLE: Genetic models of obesity and energy balance in the mouse.
AUTHOR: Robinson S.W.; Dinulescu D.M.; Cone R.D.
CORPORATE SOURCE: S.W. Robinson, Vollum Institute, Oregon Health Sciences University, 3181 SW Sam Jackson Park Road, Portland, OR 97201, United States. cone@ohsu.edu
SOURCE: Annual Review of Genetics, (2000) 34/- (687-745).
Refs: 278
ISSN: 0066-4197 CODEN: ARVGB7
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Obesity is a health problem of epidemic proportions in the industrialized world. The **cloning** and characterization of the **genes** for the five naturally occurring monogenic obesity syndromes in the mouse have led to major breakthroughs in understanding the physiology of energy

balance and the contribution of genetics to obesity in the **human** population. However, the regulation of energy balance is an extremely complex process, and it is quickly becoming clear that hundreds of **genes** are involved. In this article, we review the naturally occurring monogenic and polygenic obese mouse strains, as well as the large number of transgenic and knockout mouse models currently available for the study of obesity and energy balance.

L29 ANSWER 14 OF 46 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:172449 BIOSIS
DOCUMENT NUMBER: PREV200000172449
TITLE: Regulation of the fatty acid synthase promoter by insulin.
AUTHOR(S): Sul, Hei Sook [Reprint author]; Latasa, Maria-Jesus; Moon, Yangsoo; Kim, Kee-Hong
CORPORATE SOURCE: Department of Nutritional Sciences, University of California, Berkeley, CA, 94720, USA
SOURCE: Journal of Nutrition, (Feb., 2000) Vol. 130, No. 2 suppl., pp. 315S-320S. print.
CODEN: JONUAI. ISSN: 0022-3166.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 3 May 2000
Last Updated on STN: 4 Jan 2002

AB Expression of critical enzymes in fatty acid and fat biosynthesis is tightly controlled by nutritional and hormonal stimuli. The expression of fatty acid synthase, which catalyzes all reactions for synthesis of palmitate from acetyl-CoA and malonyl-CoA, and of mitochondrial **glycerol**-3-phosphate **acyltransferase**, which catalyzes the first acylation step in glycerophospholipid synthesis, is decreased to an undetectable level during fasting. Food intake, especially a high carbohydrate, fat-free diet after fasting, causes a dramatic increase in the transcription of these **genes**. Insulin secretion is increased during feeding and has a positive effect on expression. By using adipocytes in culture and transgenic mice that express the reporter **gene** driven by the fatty acid synthase promoter, the cis-acting sequence that mediates insulin regulation of the fatty acid synthase promoter was defined. Upstream stimulatory factors (USF) that bind to the -65 E-box are required for insulin-mediated transcriptional activation of the fatty acid symthase **gene**. Sterol regulatory element binding protein (SREBP)-1 may be also involved in induction of these **genes** during feeding. Using specific inhibitors and expressing various signaling molecules, we found that insulin regulation of the fatty acid synthase promoter is mediated by the phosphatidylinositol (PI)3-kinase signaling pathway and that protein kinase B/akt is a downstream effector.

L29 ANSWER 15 OF 46 MEDLINE on STN
ACCESSION NUMBER: 2000069349 MEDLINE
DOCUMENT NUMBER: 20069349 PubMed ID: 10601854
TITLE: Expression in yeast and tobacco of plant **cDNAs** encoding acyl CoA:diacylglycerol **acyltransferase**.
AUTHOR: Bouvier-Nave P; Benveniste P; Oelkers P; Sturley S L; Schaller H
CORPORATE SOURCE: Institut de Biologie Moleculaire des Plantes, Strasbourg, France.. Pierre.Benveniste@ibmp-ulp.u-strasbg.fr
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (2000 Jan) 267 (1) 85-96.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AC003058; GENBANK-AC005917
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000229
Last Updated on STN: 20000229
Entered Medline: 20000215

AB During the course of a search for **cDNAs** encoding plant sterol **acyltransferases**, an expressed sequence tag **clone** presenting substantial identity with yeast and animal acyl CoA:cholesterol **acyltransferases** was used to screen **cDNA** libraries from Arabidopsis and tobacco. This resulted in the isolation of two full-length **cDNAs** encoding proteins of 520 and 532 amino acids,

respectively. Attempts to complement the yeast double-mutant are1 are2 defective in acyl CoA:cholesterol **acyltransferase** were unsuccessful, showing that neither **gene** encodes acyl CoA:cholesterol **acyltransferase**. Their deduced amino acid sequences were then shown to have 40 and 38% identity, respectively, with a murine acyl CoA:diacylglycerol **acyltransferase** and their expression in are1 are2 or wild-type yeast resulted in a strong increase in the incorporation of oleyl CoA into triacylglycerols. Incorporation was 2-3 times higher in microsomes from yeast transformed with these plant **cDNAs** than in yeast transformed with the void vector, clearly showing that these **cDNAs** encode acyl CoA:diacylglycerol **acyltransferases**. Moreover, during the preparation of microsomes from the Arabidopsis DGAT-transformed yeast, a floating layer was observed on top of the 100 000 g supernatant. This fraction was enriched in triacylglycerols and exhibited strong acyl CoA:diacylglycerol **acyltransferase** activity, whereas almost no activity was detected in the corresponding clear fraction from the control yeast. Thanks to the use of this active fraction and dihexanoylglycerol as a substrate, the de novo synthesis of 1,2-dihexanoyl 3-oleyl **glycerol** by AtDGAT could be demonstrated. Transformation of tobacco with AtDGAT was also performed. Analysis of 19 primary transformants allowed detection, in several individuals, of a marked increase (up to seven times) of triacylglycerol content which correlated with the AtDGAT mRNA expression. Furthermore, light-microscopy observations of leaf epidermis cells, stained with a lipid-specific dye, showed the presence of lipid droplets in the cells of triacylglycerol-overproducer plants, thus illustrating the potential application of acyl CoA:diacylglycerol **acyltransferase** -transformed plants.

L29 ANSWER 16 OF 46 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000333914 EMBASE
TITLE: Physiological and nutritional regulation of enzymes of triacylglycerol synthesis.
AUTHOR: Coleman R.A.; Lewin T.M.; Muoio D.M.
CORPORATE SOURCE: R.A. Coleman, Department of Nutrition, University of North Carolina, Chapel Hill, NC 27599, United States. rcoleman@sph.unc.edu
SOURCE: Annual Review of Nutrition, (2000) 20/- (77-103). Refs: 165 ISSN: 0199-9885 CODEN: ARNTD8
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 002 Physiology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Although triacylglycerol stores play the critical role in an organism's ability to withstand fuel deprivation and are strongly associated with such disorders as diabetes, obesity, and atherosclerotic heart disease, information concerning the enzymes of triacylglycerol synthesis, their regulation by hormones, nutrients, and physiological conditions, their mechanisms of action, and the roles of specific isoforms has been limited by a lack of **cloned cDNAs** and purified proteins. Fortunately, molecular tools for several key enzymes in the synthetic pathway are becoming available. This review summarizes recent studies of these enzymes, their regulation under varying physiological conditions, their purported roles in synthesis of triacylglycerol and related glycerolipids, the possible functions of different isoenzymes, and the evidence for specialized cellular pools of triacylglycerol and glycerolipid intermediates.

L29 ANSWER 17 OF 46 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:682053 CAPLUS
DOCUMENT NUMBER: 132:21767
TITLE: Increased levels of nuclear SREBP-1c associated with fatty livers in two mouse models of diabetes mellitus
AUTHOR(S): Shimomura, Iichiro; Bashmakov, Yuriy; Horton, Jay D.
CORPORATE SOURCE: Department of Molecular Genetics, University of Texas Southwestern Medical Center, Dallas, TX, 75235-9046, USA

SOURCE: Journal of Biological Chemistry (1999), 274(42), 30028-30032
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hepatic steatosis is common in non-insulin-dependent diabetes and can be assocd. with fibrosis and cirrhosis in a subset of individuals. Increased rates of fatty acid synthesis have been reported in livers from rodent models of diabetes and may contribute to the development of steatosis. Sterol regulatory element-binding proteins (SREBPs) are a family of regulated transcription factors that stimulate lipid synthesis in liver. In the current studies, we measured the content of SREBPs in livers from two mouse models of diabetes, obese ob/ob mice and transgenic aP2-SREBP-1c436 (aP2-SREBP-1c) mice that overexpress nuclear SREBP-1c only in adipose tissue. The aP2-SREBP-1c mice exhibit a syndrome that resembles congenital generalized lipodystrophy in **humans**. Both lines of mice develop hyperinsulinemia, hyperglycemia, and hepatic steatosis. Nuclear SREBP-1c protein levels were significantly elevated in livers from ob/ob and aP2-SREBP-1c mice compared with wild-type mice. Increased nuclear SREBP-1c protein was assocd. with elevated mRNA levels for known SREBP target **genes** involved in fatty acid biosynthesis, which led to significantly higher rates of hepatic fatty acid synthesis in vivo. These studies suggest that increased levels of nuclear SREBP-1c contribute to the elevated rates of hepatic fatty acid synthesis that leads to steatosis in diabetic mice.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 18 OF 46 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 1999362265 EMBASE
TITLE: A proteolytic pathway that controls the cholesterol content of membranes, cells, and blood.
AUTHOR: Brown M.S.; Goldstein J.L.
CORPORATE SOURCE: M.S. Brown, Department of Molecular Genetics, Texas Univ. Southwestern Med. Center, 5323 Harry Hines Boulevard, Dallas, TX 75235, United States. mbrowl@mednet.swmed.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (28 Sep 1999) 96/20 (11041-11048).
Refs: 60
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The integrity of cell membranes is maintained by a balance between the amount of cholesterol and the amounts of unsaturated and saturated fatty acids in phospholipids. This balance is maintained by membrane-bound transcription factors called sterol regulatory element-binding proteins (SREBPs) that activate **genes** encoding enzymes of cholesterol and fatty acid biosynthesis. To enhance transcription, the active NH2-terminal domains of SREBPs are released from endoplasmic reticulum membranes by two sequential cleavages. The first is catalyzed by Site-1 protease (S1P), a membrane-bound subtilisin-related serine protease that cleaves the hydrophilic loop of SREBP that projects into the endoplasmic reticulum lumen. The second cleavage, at Site-2, requires the action of S2P, a hydrophobic protein that appears to be a zinc metalloprotease. This cleavage is unusual because it occurs within a membrane-spanning domain of SREBP. Sterols block SREBP processing by inhibiting S1P. This response is mediated by SREBP cleavage-activating protein (SCAP), a regulatory protein that activates S1P and also serves as a sterol sensor, losing its activity when sterols overaccumulate in cells. These regulated proteolytic cleavage reactions are ultimately responsible for controlling the level of cholesterol in membranes, cells, and blood.

L29 ANSWER 19 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2000:182977 SCISEARCH
THE GENUINE ARTICLE: BP58H
TITLE: **cDNA cloning**, expression and chromosomal localization of two **human** lysophosphatidic acid **acyltransferases**
AUTHOR: Eberhardt C (Reprint); Gray P W; Tjoelker L W
CORPORATE SOURCE: ICOS CORP, BOTHELL, WA 98021 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY, (DEC 1999) Vol. 469, pp. 351-356.
Publisher: KLUWER ACADEMIC / PLENUM PUBL, 233 SPRING ST, NEW YORK, NY 10013.
ISSN: 0065-2598.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 18

L29 ANSWER 20 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 1999:896353 SCISEARCH
THE GENUINE ARTICLE: 256EW
TITLE: Peroxisome proliferators as adjuvants for the reverse-electron-transport therapy of obesity: an explanation for the large increase in metabolic rate of MEDICA 16-treated rats
AUTHOR: McCarty M F (Reprint)
CORPORATE SOURCE: NUTRIGUARD RES, 1051 HERMES AVE, ENCINITAS, CA 92024 (Reprint); NUTR 21 AMBI, SAN DIEGO, CA 92109
COUNTRY OF AUTHOR: USA
SOURCE: MEDICAL HYPOTHESES, (OCT 1999) Vol. 53, No. 4, pp. 272-276
.
Publisher: CHURCHILL LIVINGSTONE, JOURNAL PRODUCTION DEPT, ROBERT STEVENSON HOUSE, 1-3 BAXTERS PLACE, LEITH WALK, EDINBURGH EH1 3AF, MIDLOTHIAN, SCOTLAND.
ISSN: 0306-9877.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 61
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The efficacy of reverse-electron-transport: therapy of obesity should be promoted by agents which upregulate hepatocyte enzymes that are potentially rate-limiting for mitochondrial fatty acid oxidation and electron shuttles. Peroxisome proliferator drugs, including the fibrates used to treat hyperlipidemia, may be useful in this regard, as they induce malic enzyme, the mitochondria[**glycerol**-3-phosphate dehydrogenase, and carnitine palmitoyl transferase I in rodent hepatocytes. An agent of this class, MEDICA 16, has the additional property of potently inhibiting both citrate lyase and acetyl-CoA carboxylase. As a result, methyl-substituted diacarboxylic acids (MEDICA) 16 can be expected to disinhibit hepatic fatty acid oxidation while up-regulating electron shuttle mechanisms, and thus should stimulate reverse electron transport. This may explain the remarkable 40% increase in basal metabolic rate observed in normal rats ingesting MEDICA 16 - an effect not associated with any compensatory increase in food intake. Relative to controls, the MEDICA 16-treated rats achieved a 50% reduction in body fat and a modest increase in lean mass, such that weight and growth were not changed. In other rodent strains, MEDICA 16 has prevented obesity diabetes and atherogenesis. However, whether MEDICA 16 and other peroxisome proliferator drugs will have clinical utility in reverse-electron-transport therapy may hinge on their ability to induce key enzymes in **human** hepatocytes; cell culture studies to evaluate this am required. (C) 1999 Harcourt Publishers Ltd.

L29 ANSWER 21 OF 46 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:413258 BIOSIS
DOCUMENT NUMBER: PREV199800413258
TITLE: Nutritional and hormonal regulation of enzymes in fat synthesis: Studies of fatty acid synthase and mitochondrial **glycerol**-3-phosphate **acyltransferase** **gene** transcription.
AUTHOR(S): Sul, Hei Sook; Wang, Dong

CORPORATE SOURCE: Dep. Nutr. Sci., Univ. Calif., Berkeley, CA 94720, USA
SOURCE: McCormick, D. B. [Editor]. Annu. Rev. Nutr., (1998) pp. 331-351. Annual Review of Nutrition. print.
Publisher: Annual Reviews Inc., P.O. Box 10139, 4139 El Camino Way, Palo Alto, California 94306, USA. Series: Annual Review of Nutrition.
CODEN: ARNTD8. ISSN: 0199-9885. ISBN: 0-8243-2818-3.
DOCUMENT TYPE: Book
Book; (Book Chapter)
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 2 Oct 1998
Last Updated on STN: 2 Oct 1998

L29 ANSWER 22 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 1998:165266 SCISEARCH
THE GENUINE ARTICLE: YX516
TITLE: Characterization of a **human** lysophosphatidic acid **acyltransferase** that is encoded by a **gene** located in the class III region of the **human** major histocompatibility complex
AUTHOR: Aguado B; Campbell R D (Reprint)
CORPORATE SOURCE: UNIV OXFORD, DEPT BIOCHEM, MRC, IMMUNOCHEM UNIT, S PARKS RD, OXFORD OX1 3QU, ENGLAND (Reprint); UNIV OXFORD, DEPT BIOCHEM, MRC, IMMUNOCHEM UNIT, OXFORD OX1 3QU, ENGLAND
COUNTRY OF AUTHOR: ENGLAND
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (13 FEB 1998) Vol. 273, No. 7, pp. 4096-4105.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 44
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Sequence analysis of **cDNA clones** corresponding to a number of **genes** located in the class III region of the **human** major histocompatibility complex (MHC), in the chromosome band 6p21.3, has shown that the G15 **gene** encodes a 283-amino acid polypeptide with significant homology over the entire polypeptide with the enzyme lysophosphatidic acid **acyltransferase** (LPAAT) from different yeast, plant, and bacterial species, The amino acid sequence of the MHC-encoded **human** LPAAT (hLPAAT alpha) is 48% identical to the recently described hLPAAT (Eberhardt, C., Gray, P. W., and Tjoelker, L. W. (1991) J, Biol. Chem. 272, 20299 - 20305), which is encoded by a **gene** located on chromosome 9p34.3, LPAAT is the enzyme that in lipid metabolism converts lysophosphatidic acid (LPA) into phosphatidic acid (PA), The expression of the hEPAAT alpha polypeptide in the baculovirus system and in mammalian cells has shown that it is an intracellular protein that contains LPAAT activity. Cell extracts from insect cells overexpressing hLPAAT alpha were analyzed in different LPAAT enzymatic assays using as substrates, different acyl acceptors and acyl donors, These cell extracts were found to contain up to 5-fold more LPAAT activity compared with control cell extracts, indicating that the hLPAAT alpha specifically converts LPA into PA, incorporating different acyl-CoAs with different affinities, The hLPAAT alpha polypeptide expressed in the mammalian Chinese hamster ovary cell Pine was found, by confocal immunofluorescence, to be localized in the endoplasmic reticulum, Due to the known role of EPA anti PA in intracellular signaling and inflammation, the hLPAAT alpha **gene** represents a candidate **gene** for some MHC-associated diseases.

L29 ANSWER 23 OF 46 EMBASE
on STN
ACCESSION NUMBER: 1998402413 EMBASE
TITLE: Eukaryotic lipid-biosynthetic enzymes: The same but not the same.
AUTHOR: Vance J.E.
CORPORATE SOURCE: J.E. Vance, Lipid and Lipoprotein Research Group, University of Alberta, Edmonton, Alta. T6G 2S2, Canada.

jean.vance@ualberta.ca
SOURCE: Trends in Biochemical Sciences, (1998) 23/11 (423-428).
Refs: 39
ISSN: 0968-0004 CODEN: TBSCDB
PUBLISHER IDENT.: S 0968-0004(98)01297-3
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The discovery that different eukaryotic enzymes catalyse the same lipid-biosynthetic reaction has paralleled the recognition that segregated pools of lipids have unique biological functions. This review considers enzymes involved in the synthesis of diverse classes of lipids-glycerolipid precursors, phospholipids, sterols and eicosanoids-and summarizes recent data that show that these duplicate enzymes are frequently encoded by different **genes** and have unique subcellular locations. Does this duality merely represent redundancy or do the different isoforms provide pools of lipids for specific biological purposes? Copyright (C) 1998 Elsevier Science Ltd.

L29 ANSWER 24 OF 46 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1998:464137 BIOSIS
DOCUMENT NUMBER: PREV199800464137
TITLE: The role of lysophosphatide **acyltransferases** and protein kinase C isoforms in the regulation of lymphocyte responses.
AUTHOR(S): Szamel, M. [Reprint author]; Kaever, V.; Leufgen, H.; Resch, K.
CORPORATE SOURCE: Inst. Mol. Pharmacol., Med. Sch. Hannover, PO Box 61 01 80, D-30625 Hannover, Germany
SOURCE: Biochemical Society Transactions, (Aug., 1998) Vol. 26, No. 3, pp. 370-374. print.
Meeting Info.: 665th Meeting of the Biochemical Society. Southampton, England, UK. March 31-April 2, 1998. Biochemical Society.
CODEN: BCSTB5. ISSN: 0300-5127.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Paper)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Oct 1998
Last Updated on STN: 30 Oct 1998

L29 ANSWER 25 OF 46 MEDLINE on STN
ACCESSION NUMBER: 1998371502 MEDLINE
DOCUMENT NUMBER: 98371502 PubMed ID: 9706228
TITLE: Nutritional and hormonal regulation of enzymes in fat synthesis: studies of fatty acid synthase and mitochondrial **glycerol**-3-phosphate **acyltransferase** **gene** transcription.
AUTHOR: Sul H S; Wang D
CORPORATE SOURCE: Department of Nutritional Sciences, University of California, Berkeley 94720, USA.. hsul@nature.berkeley.edu
CONTRACT NUMBER: DK36264 (NIDDK)
SOURCE: ANNUAL REVIEW OF NUTRITION, (1998) 18 331-51. Ref: 139
Journal code: 8209988. ISSN: 0199-9885.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 19981029
Last Updated on STN: 19981029
Entered Medline: 19981022
AB The activities of critical enzymes in fatty acid and triacylglycerol biosynthesis are tightly controlled by different nutritional, hormonal, and developmental conditions. Feeding previously fasted animals high-carbohydrate, low-fat diets causes a dramatic induction of enzymes-such as fatty acid synthase (FAS) and mitochondrial

glycerol-3-phosphate **acyltransferase** (GPAT)-involved in fatty acid and triacylglycerol synthesis. During fasting and refeeding, transcription of these two enzymes is coordinately regulated by nutrients and hormones, such as glucose, insulin, glucagon, glucocorticoids, and thyroid hormone. Insulin stimulates transcription of the FAS and mitochondrial GPAT **genes**, and glucagon antagonizes the insulin effect through the cis-acting elements within the promoters and their bound trans-acting factors. This review discusses advances made in the understanding of the transcriptional regulation of FAS and mitochondrial GPAT **genes**, with emphasis on elucidation of the mechanisms by which multiple nutrients and hormones achieve their effects.

L29 ANSWER 26 OF 46 MEDLINE on STN
ACCESSION NUMBER: 1998256934 MEDLINE
DOCUMENT NUMBER: 98256934 PubMed ID: 9594578
TITLE: Regulation of fat synthesis and adipose differentiation.
AUTHOR: Sul H S; Smas C M; Wang D; Chen L
CORPORATE SOURCE: Department of Nutritional Sciences, University of California, Berkeley 94720-3104, USA.
CONTRACT NUMBER: DK36264 (NIDDK)
DK50828 (NIDDK)
SOURCE: PROGRESS IN NUCLEIC ACID RESEARCH AND MOLECULAR BIOLOGY, (1998) 60 317-45. Ref: 76
Journal code: 0102753. ISSN: 0079-6603.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980625
Last Updated on STN: 19980625
Entered Medline: 19980615

AB Adipocytes have highly specialized function of accumulating fat as stored energy that can be used during periods of food deprivation. The process of fat synthesis and development of adipose tissue are under hormonal and nutritional control. This review first describes transcription of the two critical enzymes involved in fat synthesis, fatty acid synthase and mitochondrial **glycerol**-3-phosphate **acyltransferase**, is decreased to an undetectable level during fasting. Food intake, especially a high carbohydrate, fat-free diet, subsequent to fasting causes dramatic increase in transcription of these **genes**. Insulin secretion is increased during feeding, having a positive effect, whereas cAMP, which mediates the effect of glucagon which increases during fasting, has a negative effect on transcription of these **genes**. Using adipocytes in culture and in transgenic mice that express liciferase driven by the fatty acid synthase promoter, cis-acting and trans-acting factors that may mediate the transcriptional regulation were examined. Upstream stimulatory factors (USFs) that bind to -65 E-box are required for insulin-mediated transcriptional activation of the fatty acid synthase **gene**. This review next describes how pref-1 is a novel inhibitor of adipose differentiation and is a plasma membrane protein containing six EGF-repeats in the extracellular domain. Pref-1 is highly expressed in 3T3-L1 preadipocytes, but is not detectable in mature fat cells. Down regulation of pref-1 is required for adipose differentiation, and constitutive expression of pref-1 inhibits adipogenesis. Moreover, the ectodomain of pref-1 is cleaved to generate a biologically active 50 kDa soluble form. There are four major forms of membrane pref-1 resulting from alternate splicing, but two of the forms with a larger deletion do not produce biologically active soluble form, indicating that alternate splicing determines the range of action, juxtacrine or paracrine, of the pref-1.

L29 ANSWER 27 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:604973 SCISEARCH
THE GENUINE ARTICLE: XQ059
TITLE: **Human** lysophosphatidic acid **acyltransferase - cDNA cloning**, expression, and localization to chromosome 9q34.3
AUTHOR: Eberhardt C; Gray P W; Tjoelker L W (Reprint)

CORPORATE SOURCE: ICOS CORP, 22021 20TH AVE SE, BOTHELL, WA 98021 (Reprint); ICOS CORP, BOTHELL, WA 98021
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (8 AUG 1997) Vol. 272, No. 32, pp. 20299-20305. Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814. ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 44

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Lysophosphatidic acid (1-acyl-sn-glycero-3-phosphate (LPA)) is a phospholipid with diverse biological activities. The mediator serves as an intermediate in membrane phospholipid metabolism but is also produced in acute settings by activated platelets. LPA is converted to phosphatidic acid, itself a lipid mediator, by an LPA **acyltransferase** (LPAAT). A **human** expressed sequence tag was identified by homology with a coconut LPAAT and used to isolate a full-length **human cDNA** from a heart muscle library. The predicted amino acid sequence bears 33% identity with a Caenorhabditis elegans LPAAT homologue and 23-28% Identity with plant and prokaryotic LPAATs. Recombinant protein produced in COS 7 cells exhibited LPAAT activity with a preference for LPA as the acceptor phosphoglycerol and arachidonyl coenzyme A as the acyl donor. Northern blotting demonstrated that the mRNA is expressed in most **human** tissues including a panel of brain subregions; expression is highest in liver and pancreas and lowest in placenta. The **human** LPAAT **gene** is contained on six exons that map to chromosome 9, region q34.3.

L29 ANSWER 28 OF 46 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 97207292 MEDLINE
DOCUMENT NUMBER: 97207292 PubMed ID: 9054427
TITLE: Identification of **glycerol**-3-phosphate **acyltransferase** as an adipocyte determination and differentiation factor 1- and sterol regulatory element-binding protein-responsive **gene**.
AUTHOR: Ericsson J; Jackson S M; Kim J B; Spiegelman B M; Edwards P A
CORPORATE SOURCE: Department of Biological Chemistry, UCLA, Los Angeles, California 90095, USA.
CONTRACT NUMBER: 2R371DK31405 (NIDDK) HL 30568 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Mar 14) 272 (11) 7298-305. Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199704
ENTRY DATE: Entered STN: 19970424
Last Updated on STN: 19980206
Entered Medline: 19970417

AB We demonstrate that the mRNA levels of **glycerol**-3-phosphate **acyltransferase** (GPAT), a mitochondrial enzyme catalyzing the initial step in glycerolipid synthesis, are induced during the differentiation of 3T3-L1 preadipocytes to adipocytes and following ectopic expression of rat adipocyte determination and differentiation factor 1 (ADD1), a protein with high homology to the **human** sterol regulatory element-binding protein-1 (SREBP-1). The increase in GPAT mRNA levels that occurs during differentiation is partially prevented by ectopic expression of a dominant negative form of ADD1. Nucleotide sequences corresponding to the proximal promoter of the murine mitochondrial GPAT **gene** (Jerkins, A. A., Liu, W. R., Lee, S., and Sul, H. S. (1995) J. Biol. Chem. 270, 1416-1421) bound SREBP-1a and NF-Y in electromobility shift assays. In addition, GPAT promoter-luciferase reporter **genes** were stimulated by co-expression of SREBP-1a. This increase was attenuated when either a dominant negative form of NF-Y was co-transfected into the cells or when

the GPAT promoter contained mutations in the putative binding sites for SREBP-1a or NF-Y. These studies demonstrate that the regulated expression of the mitochondrial GPAT **gene** requires both NF-Y and ADD1/SREBPs. Thus, SREBPs/ADD1 regulate not only **genes** involved in cholesterol homeostasis and fatty acid synthesis but also a key enzyme in glycerolipid synthesis.

L29 ANSWER 29 OF 46 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 97355682 MEDLINE
DOCUMENT NUMBER: 97355682 PubMed ID: 9212163
TITLE: **Cloning** and expression of two **human** lysophosphatidic acid **acyltransferase** **cDNAs** that enhance cytokine-induced signaling responses in cells.
AUTHOR: West J; Tompkins C K; Balantac N; Nudelman E; Meengs B; White T; Bursten S; Coleman J; Kumar A; Singer J W; Leung D W
CORPORATE SOURCE: Cell Therapeutics, Inc., Seattle, WA 98119, USA.
SOURCE: DNA AND CELL BIOLOGY, (1997 Jun) 16 (6) 691-701.
Journal code: 9004522. ISSN: 1044-5498.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U56417; GENBANK-U56418; GENBANK-U89336
ENTRY MONTH: 199707
ENTRY DATE: Entered STN: 19970812
Last Updated on STN: 19970812
Entered Medline: 19970725

AB Lysophosphatidic acid (LPA) and phosphatidic acid (PA) are two phospholipids involved in signal transduction and in lipid biosynthesis in cells. LPA **acyltransferase** (LPAAT), also known as 1-acyl sn-**glycerol**-3-phosphate acetyltransferase (EC 2.3.1.51), catalyzes the conversion of LPA to PA. In this study, we describe the isolation and characterization of two **human** **cDNAs** that encode proteins possessing LPAAT activities. These two proteins, designated here as LPAAT-alpha and LPAAT-beta, contain extensive sequence sequence similarities to microbial or plant LPAAT sequences. LPAAT-alpha mRNA was detected in all tissues with highest expression in skeletal muscle whereas LPAAT-beta was expressed predominantly in heart and liver tissues. Expression of these two **cDNAs** in an Escherichia coli strain with a mutated LPAAT **gene** (plsC) complements its growth defect and shifts the equilibrium of cellular lipid content from LPA to PA and other lipids. Overexpression of these two **cDNAs** in mammalian cells leads to increased LPAAT activity in cell-free extracts using an in vitro assay that measures the conversion of fluorescently labeled LPA to PA. This increase in LPAAT activity correlates with enhancement of transcription and synthesis of tumor necrosis factor-alpha and interleukin-6 from cells upon stimulation with interleukin-1beta, suggesting LPAAT overexpression may amplify cellular signaling responses from cytokines.

L29 ANSWER 30 OF 46 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 97445095 MEDLINE
DOCUMENT NUMBER: 97445095 PubMed ID: 9299423
TITLE: **cDNA cloning** and expression of murine 1-acyl-sn-**glycerol**-3-phosphate **acyltransferase**.
AUTHOR: Kume K; Shimizu T
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Tokyo, Japan.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1997 Aug 28) 237 (3) 663-6.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB005623; GENBANK-L13282; GENBANK-M63491; GENBANK-T77083; GENBANK-U89336
ENTRY MONTH: 199710

ENTRY DATE: Entered STN: 19971024
Last Updated on STN: 19990129
Entered Medline: 19971015

AB 1-Acyl-sn-**glycerol**-3-phosphate (1-AGP), also known as lysophosphatidic acid (LPA), is an intermediate of de novo biosynthesis of glycerophospholipids and triacylglycerol. LPA is also attracting much attention because of its growth stimulating effects. Here we report **cloning** of murine **cDNA** encoding 1-AGP **acyltransferase** (1-AGPAT), which converts LPA into phosphatidic acid by incorporating acyl moiety at an-2 position. The **cDNA** contains an open reading frame coding for 285 amino acids, with highly hydrophobic regions in the N-terminal half. The Northern blot analysis using various mouse tissues revealed ubiquitous expressions of two transcripts. The **cDNA** was expressed in Escherichia coli JC201, a plsC mutant strain deficient in the 1-AGPAT activity, and the enzyme properties were examined. The enzyme utilized both saturated and unsaturated acyl-CoA as an acyl-donor, while it utilized LPA but not other lysophospholipids as an acceptor.

L29 ANSWER 31 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 1998:44464 SCISEARCH
THE GENUINE ARTICLE: YN849
TITLE: **Human** lysophosphatidic acid **acyltransferase** is encoded by a **gene** located in the Major Histocompatibility Complex.
AUTHOR: Aguado B (Reprint); Campbell R D
CORPORATE SOURCE: UNIV OXFORD, DEPT BIOCHEM, MRC, IMMUNOCHEM UNIT, S PARKS RD, OXFORD OX1 3QU, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND
SOURCE: BIOCHEMICAL SOCIETY TRANSACTIONS, (NOV 1997) Vol. 25, No. 4, pp. S597-S597.
Publisher: PORTLAND PRESS, 59 PORTLAND PLACE, LONDON, ENGLAND W1N 3AJ.
ISSN: 0300-5127.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 10

L29 ANSWER 32 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:456490 SCISEARCH
THE GENUINE ARTICLE: XD377
TITLE: Triacsin C blocks de novo synthesis of glycerolipids and cholesterol esters but not recycling of fatty acid into phospholipid: Evidence for functionally separate pools of acyl-CoA
AUTHOR: Igal R A (Reprint); Wang P; Coleman R A
CORPORATE SOURCE: UNIV N CAROLINA, DEPT NUTR, CHAPEL HILL, NC 27599 (Reprint); UNIV N CAROLINA, DEPT PEDIAT, CHAPEL HILL, NC 27599
COUNTRY OF AUTHOR: USA
SOURCE: BIOCHEMICAL JOURNAL, (1 JUN 1997) Vol. 324, Part 2, pp. 529-534.
Publisher: PORTLAND PRESS, 59 PORTLAND PLACE, LONDON, ENGLAND W1N 3AJ.
ISSN: 0264-6021.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 26

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The trafficking of acyl-CoAs within cells is poorly understood. In order to determine whether newly synthesized acyl-CoAs are equally available for the synthesis of all glycerolipids and cholesterol esters, we incubated **human** fibroblasts with [C-14]oleate, [H-3]arachidonate or [H-3]**glycerol** in the presence or absence of triacsin C, a fungal metabolite that is a competitive inhibitor of acyl-CoA synthetase. Triacsin C inhibited de novo synthesis from **glycerol** of triacylglycerol, diacylglycerol and cholesterol esters by more than 93%, and the synthesis of phospholipid by 83%. However, the incorporation of oleate or arachidonate into phospholipids appeared to be

relatively unimpaired when triacsin was present. Diacylglycerol **acyltransferase** and lysophosphatidylcholine **acyltransferase** had similar dependences on palmitoyl-CoA in both liver and fibroblasts; thus it did not appear that acyl-CoAs, when present at low concentrations, would be preferentially used to acylate lysophospholipids. We interpret these data to mean that, when fatty acid is not limiting, triacsin blocks the acylation of **glycerol** 3-phosphate and diacylglycerol, but not the reacylation of lysophospholipids. Two explanations are possible: (1) different acyl-CoA synthetases exist that vary in their sensitivity to triacsin; (2) an independent mechanism channels acyl-CoA towards phospholipid synthesis when little acyl-CoA is available. In either case, the acyl-CoAs available to acylate cholesterol, **glycerol** 3-phosphate, lysophosphatidic acid and diacylglycerol and those acyl-CoAs that are used by lysophospholipid **acyltransferases** and by ceramide N-**acyltransferase** must reside in two non-mixing acyl-CoA pools or, when acyl-CoAs are limiting, they must be selectively channelled towards specific **acyltransferase** reactions.

L29 ANSWER 33 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 97:672338 SCISEARCH
THE GENUINE ARTICLE: XU411
TITLE: A **human cDNA** sequence with homology to non-mammalian lysophosphatidic acid **acyltransferases**
AUTHOR: Stamps A C (Reprint); Elmore M A; Hill M E; Kelly K; Makda A A; Finnen M J
CORPORATE SOURCE: YAMANOUCHI RES INST, LITTLEMORE PK, OXFORD OX4 4SX, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND
SOURCE: BIOCHEMICAL JOURNAL, (1 SEP 1997) Vol. 326, Part 2, pp. 455-461.
Publisher: PORTLAND PRESS, 59 PORTLAND PLACE, LONDON, ENGLAND W1N 3AJ.
ISSN: 0264-6021.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 24
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A novel **human** homologue of Escherichia coli, yeast and plant 1-acylglycerol-3-phosphate **acyltransferase** has been isolated from U937 cell **cDNA**. Expression of the **cloned** sequence in 1-acylglycerol-3-phosphate **acyltransferase**-deficient E. coli resulted in increased incorporation of oleic acid into cellular phospholipids. Membranes made from COS7 cells transfected with the **cDNA** exhibited higher **acyltransferase** activity towards a range of donor fatty acyl-CoAs and lysophosphatidic acid. Northern-blot analysis of the **cDNA** sequence indicated high levels of expression in immune cells and epithelium. Rapid amplification of **cDNA** ends revealed differentially expressed splice variants, which suggests regulation of the enzyme by alternative splicing. This **cDNA** therefore represents the first described sequence of a mammalian **gene** homologous to non-mammalian lysophosphatidic acid **acyltransferases**.

L29 ANSWER 34 OF 46 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:6150 CAPLUS
DOCUMENT NUMBER: 132:307079
TITLE: Characterisation of the G15 **gene** located between the class II region and the C4 **genes** in the **human** MHC
AUTHOR(S): Aguado, B.; Campbell, R. D.
CORPORATE SOURCE: MRC Immunochemistry Unit, Oxford University, Oxford, OX1 3QU, UK
SOURCE: HLA: Genetic Diversity of HLA Functional and Medical Implication, [Proceedings of the International Histocompatibility Workshop and Conference], 12th, Saint-Malo and Paris, France, 1996 (1997), Meeting Date 1996, Volume 2, 224-227. Editor(s): Charron, Dominique. EDK, Medical and Scientific International

Publisher: Sevres, Fr.
CODEN: 68MRA5
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The novel **gene** G15 encodes a 283 amino acid protein with a predicted mol. wt. of about 32 kDa which contains putative transmembrane segments. The G15 **gene** is a single copy **gene**, found in cell lines U937, Molt4 and Raji cells. The protein shows homol. with the enzyme LPAAT (1-acyl-sn-**glycerol**-3-phosphate **acyltransferase** (lysophosphatidic acid acyl transferase) from several bacteria. The authors expressed G15 in insect cells using the baculovirus system and are trying to demonstrate by enzymic assays whether G15 is the **human** LPAAT and to identify the cellular localization of the enzyme.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 35 OF 46 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:616292 CAPLUS
DOCUMENT NUMBER: 127:316047
TITLE: Alkyl-dihydroxyacetonephosphate synthase
AUTHOR(S): van den Bosch, H.; de Vet, E. C. J. M.
CORPORATE SOURCE: Centre for Biomembranes and Lipid Enzymology, Institute of Biomembranes, Utrecht University, Padualaan 8, CH Utrecht, 3584, Neth.
SOURCE: Biochimica et Biophysica Acta (1997), 1348(1-2), 35-44
CODEN: BBACAQ; ISSN: 0006-3002
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 37 refs. Mammalian ether phospholipids are characterized by a glycero-ether linkage at the sn-1-position of the **glycerol** backbone. In **humans**, this type of phospholipid species occurs mainly in the ethanolamine and choline phosphoglycerides comprising an estd. 15% of total phospholipids. The glycero-ether linkage is synthesized by replacement of the acyl chain in acyldihydroxyacetone phosphate by a long-chain alc. that donates the oxygen for the ether linkage. Both the enzyme that forms acyldihydroxyacetone phosphate (dihydroxyacetone phosphate **acyltransferase**) and the one that introduces the glycero-ether linkage (alkyldihydroxyacetone phosphate synthase) are located in peroxisomes. The deficiency of ether phospholipids in **human** inborn errors of metab., caused by defects in peroxisome biogenesis, has clearly delineated the indispensable role of peroxisomes in ether phospholipid synthesis. The most characteristic enzyme of ether lipid synthesis is alkyldihydroxyacetone phosphate synthase. Its discovery and some of its properties, including mechanistic studies, have been discussed in recent reviews. This review recapitulates these findings and focuses on the new insights into the structure and properties of the enzyme that have recently been obtained resulting from the purifn. and subsequent **cloning** and expression of the **cDNA** encoding this peroxisomal enzyme.

L29 ANSWER 36 OF 46 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96068461 EMBASE
DOCUMENT NUMBER: 1996068461
TITLE: The PAL1 **gene** product is a peroxisomal ATP-binding cassette transporter in the yeast Saccharomyces cerevisiae.
AUTHOR: Swartzman E.E.; Viswanathan M.N.; Thorner J.
CORPORATE SOURCE: Biochemistry/Molecular Biology Div., Department of Molecular/Cell Biology, University of California, Corner of Hearst and Oxford Streets,Berkeley, CA 94720-3202, United States
SOURCE: Journal of Cell Biology, (1996) 132/4 (549-563).
ISSN: 0021-9525 CODEN: JCLBA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
029 Clinical Biochemistry
LANGUAGE: English

SUMMARY LANGUAGE: English

AB The PAL1 **gene** was isolated using PCR and degenerate oligonucleotide primers corresponding to highly conserved amino acid sequence motifs diagnostic of the ATP-binding cassette domain of the superfamily of membrane- bound transport proteins typified by mammalian multidrug resistance transporter 1 and Saccharomyces cerevisiae Ste6. The deduced PAL1 gent product is similar in length to, has the same predicted topology as, and shares the highest degree of amino acid sequence identity with two **human** proteins, adrenoleukodystrophy protein and peroxisomal membrane protein (70 kD), which are both presumptive ATP-binding cassette transporters thought to be constituents of the peroxisomal membrane. As judged by hybridization of a PAL1 probe to isolated **RNA** and by expression of a PAL1-lacZ fusion, a PAL1 transcript was only detectable when cells were grown on oleic acid, a carbon source which requires the biogenesis of functional peroxisomes for its metabolism. A pal1.DELTA. mutant grew normally on either glucose- or **glycerol** containing media; however, unlike PAL1+ cells (or the pal1.DELTA. mutant carrying the PAL1 **gene** on a plasmid), pal1.DELTA. cells were unable to grow on either a solid medium or a liquid medium containing oleic acid as the sole carbon source. Antibodies raised against a chimeric protein in which the COOH- terminal domain of Pal1 was fused to glutathione S-transferase specifically recognized a protein in extracts from wild-type cells only when grown on oleic acid; this species represents the PAL1 **gene** product because it was missing in pal1.DELTA. cells and more abundant in pal1.DELTA. cells expressing PAL1 from a multicopy plasmid. The Pal1 polypeptide was highly enriched in the organellar pellet fraction prepared from wild-type cells by differential centrifugation and comigrated upon velocity sedimentation in a Nycodenz gradient with a known component of the peroxisomal matrix, 3-oxoacyl-CoA thiolase. As judged by both subcellular fractionation and indirect immunofluorescence, localization of 3-oxoacyl-CoA thiolase to peroxisomes was unchanged whether Pal1 was present, absent, or overexpressed. These findings demonstrate that Pal1 is a peroxisome-specific protein, that it is required for peroxisome function, but that it is not necessary for the biogenesis of peroxisomes or for the import of 3-oxoacyl-CoA thiolase (and at least two other peroxisomal matrix proteins).

L29 ANSWER 37 OF 46 LIFESCI COPYRIGHT 2004 CSA on STN DUPLICATE 8

ACCESSION NUMBER: 95:102366 LIFESCI

TITLE: Caco-2 cells as a model for intestinal lipoprotein synthesis and secretion

AUTHOR: Levy, E.; Mehran, M.; Seidman, E.

CORPORATE SOURCE: Gastroenterol.-Nutr. Unit, Pediatr. Res. Cent., Hop. Sainte-Justine, 3175 Cote Ste-Catherine Rd., Montreal, PQ H3T 1C5, Canada

SOURCE: FASEB J., (1995) vol. 9, no. 8, pp. 626-635. ISSN: 0892-6638.

DOCUMENT TYPE: Journal

TREATMENT CODE: General Review

FILE SEGMENT: N

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Caco-2 cells, an intestinal cell line derived from a **human** colorectal carcinoma that spontaneously differentiates under standard culture conditions, lends itself to the in vitro study of **human** gut in view of its efficient intestinal transport processes. Among its multiple biological functions are those related to the absorption, transport, and metabolism of lipids and lipoproteins. Despite their intestinal origin, confluent Caco-2 cell monolayers primarily express L-FABP for the uptake of apical dietary long chain fatty acids, incorporating them into triglycerides by the **glycerol** 3-phosphate pathway, and assembling very-low-density lipoprotein, high-density lipoprotein, and low-density lipoprotein. The monoacylglycerol pathway is inactive in Caco-2 cells. Furthermore, the secretion of newly synthesized triglyceride-rich lipoproteins is very restricted, despite abundant production of apolipoprotein (apo) B. The regulation of apoB synthesis and its mRNA editing at the enterocyte level has been intensively examined in Caco-2 cells. Luminal fatty acids, calcium ion, as well as vitamins and hormones are known to modulate the apoB-48/apoB-100 at the transcriptional and/or translational level. The regulation of 3-hydroxy-3-methylglutaryl-CoA reductase and acyl-CoA:

(cholesterol **acyltransferase**), the key enzymes governing intracellular cholesterol handling, have also been extensively examined in Caco-2 cells. In many respects this cell line provides an excellent in vitro model for the investigation of intestinal lipoprotein metabolism; however, their limited secretion capacity remains a potential drawback to comparisons with the in vivo physiological state.

L29 ANSWER 38 OF 46 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 95211810 EMBASE
DOCUMENT NUMBER: 1995211810
TITLE: Eukaryotic phospholipid biosynthesis.
AUTHOR: Kent C.
CORPORATE SOURCE: Department of Biological Chemistry, University of Michigan Medical Sch.,Ann Arbor, MI 48109-0606, United States
SOURCE: Annual Review of Biochemistry, (1995) 64/- (315-343). ISSN: 0066-4154 CODEN: ARBOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The current status of the biochemistry of phospholipid biosynthesis is presented. The review focuses on the identification and characterization of molecular tools such as purified enzymes and **cloned genes** and **cDNAs** for those enzymes. The enzymes discussed are those involved in the biosynthesis of the major phospholipid classes, namely, phosphatidate, phosphatidylserine, phosphatidylethanolamine, phosphatidylcholine, sphingomyelin, phosphatidylinositol and its phosphorylated derivatives, and cardiolipin. The review centers on the pathways in mammals and yeast. Novel genetic approaches used to delineate pathways and **clone cDNAs** are discussed. The regulatory roles played by some of the enzymes involved in controlling the biosynthetic pathways are presented.

L29 ANSWER 39 OF 46 MEDLINE on STN
ACCESSION NUMBER: 94216363 MEDLINE
DOCUMENT NUMBER: 94216363 PubMed ID: 8163541
TITLE: Evidence for a lack of regulation of the assembly and secretion of apolipoprotein B-containing lipoprotein from HepG2 cells by cholesteryl ester.
AUTHOR: Wu X; Sakata N; Lui E; Ginsberg H N
CORPORATE SOURCE: Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, New York 10032.
CONTRACT NUMBER: HL 21006 (NHLBI)
HL 36000 (NHLBI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Apr 22) 269 (16) 12375-82.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
ENTRY DATE: Entered STN: 19940606
Last Updated on STN: 19980206
Entered Medline: 19940526
AB Although some previous studies have suggested that triglyceride, a major core lipid, plays a key role in the assembly and secretion of apolipoprotein B-containing lipoproteins from HepG2 cells, other reports have indicated the importance of cholesteryl ester, another core lipid. We attempted to better define the roles of triglyceride and cholesteryl ester in the assembly and secretion of apolipoprotein B-containing lipoproteins from HepG2 cells by determining the effects of Sandoz 58-035, a potent acyl-CoA **acyltransferase** inhibitor, which significantly inhibits cholesteryl synthesis, and Triacsin D, a potent fatty acyl-CoA synthetase inhibitor, which significantly inhibits triglyceride synthesis, on the secretion of apolipoprotein B-containing lipoproteins. Sandoz 58-035 (2 micrograms/ml) decreased very low density lipoproteins (VLDL)-stimulated cellular cholesteryl ester content by 60-80%, and blocked oleate-stimulated cholesteryl ester synthesis by 100%, but did not

decrease VLDL- or oleate-stimulated apolipoprotein B secretion. Triacsin D (12.5 microM), which significantly inhibited VLDL and oleate stimulation of triglyceride synthesis, without affecting cholesteryl ester synthesis, blocked the stimulation of apolipoprotein B secretion by both agents. In HepG2 cells transfected with 3-hydroxy-methylglutaryl-CoA reductase **cDNA**, cholesteryl ester synthesis and mass were increased by 100%, but apolipoprotein B secretion was unaffected. Sandoz 58-035 decreased cholesteryl ester synthesis significantly but did not decrease apolipoprotein B secretion from this cell line. When these transfected cells were incubated with oleate, apolipoprotein B secretion increased; Triacsin D blocked this effect. Finally, sphingomyelinase treatment (which shifts cholesterol from plasma membranes to intracellular pools) increased cholesteryl ester synthesis 4-5-fold, but apolipoprotein B secretion was unaffected. Changes in cellular cholesteryl ester synthesis or mass did not affect the intracellular degradation of newly synthesized apolipoprotein B, but changes in triglyceride synthesis were always associated with corresponding changes in the intracellular degradation of apolipoprotein B. In conclusion, neither long term nor short term changes in cholesteryl ester synthesis or mass regulate the assembly and secretion of apolipoprotein B-containing lipoprotein from HepG2 cells.

L29 ANSWER 40 OF 46 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 95196689 MEDLINE
DOCUMENT NUMBER: 95196689 PubMed ID: 7889876
TITLE: Hypolipidemic, anti-obesity, anti-inflammatory, anti-osteoporotic, and anti-neoplastic properties of amine carboxyboranes.
AUTHOR: Hall I H; Chen S Y; Rajendran K G; Sood A; Spielvogel B F; Shih J
CORPORATE SOURCE: Division of Medicinal Chemistry and Natural Products, School of Pharmacy, University of North Carolina Chapel Hill 27559-7360.
SOURCE: ENVIRONMENTAL HEALTH PERSPECTIVES, (1994 Nov) 102 Suppl 7 21-30. Ref: 30
Journal code: 0330411. ISSN: 0091-6765.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
ENTRY DATE: Entered STN: 19950427
Last Updated on STN: 19950427
Entered Medline: 19950420

AB The amine-carboxyborane derivatives were shown to be effective antineoplastic/cytotoxic agents with selective activity against single-cell and solid tumors derived from murine and **human** leukemias, lymphomas, sarcomas, and carcinomas. The agents inhibited **DNA** and **RNA** synthesis in preference to protein synthesis in L1210 lymphoid leukemia cells. Inosine-monophosphate dehydrogenase apparently is a target site of the compounds; similar effects on phosphoribosyl-pyrophosphate amido transferase, orotidine-monophosphate decarboxylase, and both nucleoside and nucleotide kinases were observed. Deoxyribonucleotide pool levels were reduced in the cells; **DNA** strand scission was observed with the agents. In rodents, the amine carboxyboranes were potent hypolipidemic agents, lowering both serum cholesterol and triglyceride concentrations, in addition to lowering cholesterol content of very low-density lipoprotein and low-density lipoprotein (LDL) and elevating high-density lipoprotein (HDL) cholesterol concentrations. De novo regulatory enzymes involved in lipid synthesis were also inhibited (e.g., hypocholesterolemic 3-hydroxy-3-methyl-Coenzyme A reductase, acyl-Coenzyme A cholesterol **acyltransferase**, and sn-**glycerol**-3-phosphate **acyltransferase**). Concurrently, the agents modulated LDL and HDL receptor binding, internalization, and degradation, so that less cholesterol was delivered to the plaques and more broken down from esters and conducted to the liver for biliary excretion. Tissue lipids in the aorta wall of the rat were reduced and fewer atherosclerotic morphologic lesions were present in quail aortas after treatment with the agents. Cholesterol resorption from the rat intestine was reduced in the presence of drug. Genetic

hyperlipidemic mice demonstrated the same types of reduction after treatment with the agents. The agents would effectively lower lipids in tissue based on the inhibition of regulatory enzymes in pigs. These findings should help improve domestic meat supplies from fowl and pigs. The amine-carboxyboranes were effective anti-inflammatory agents against septic shock, induced edema, pleurisy, and chronic arthritis at 2.5 to 8 mg/kg. Lysosomal and proteolytic enzyme activities were also inhibited. More significantly, the agents were dual inhibitors of prostaglandin cyclooxygenase and 5'-lipoxygenase activities. These compounds also affected cytokine release and white cell migration. Subsequent studies showed that the amine-carboxyboranes were potent anti-osteoporotic agents reducing calcium resorption as well as increasing calcium and proline incorporation into mouse pup calvaria and rat UMR-106 collagen.

L29 ANSWER 41 OF 46 MEDLINE on STN
ACCESSION NUMBER: 93299391 MEDLINE
DOCUMENT NUMBER: 93299391 PubMed ID: 8518748
TITLE: Proteins and enzymes of the peroxisomal membrane in mammals.
AUTHOR: Causeret C; Bentejac M; Bugaut M
CORPORATE SOURCE: Laboratoire de Biologie Moleculaire et Cellulaire, Faculte des Sciences Mirande, Universite de Bourgogne, Dijon, France.
SOURCE: BIOLOGY OF THE CELL, (1993) 77 (1) 89-104. Ref: 215
Journal code: 8108529. ISSN: 0248-4900.
PUB. COUNTRY: France
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199307
ENTRY DATE: Entered STN: 19930813
Last Updated on STN: 19930813
Entered Medline: 19930729

AB Proteins of the peroxisomal membrane can be schematically divided into two groups, one being made up of more or less characterized proteins with generally unknown functions and the other consisting of enzyme activities of which the corresponding proteins have not been characterized. In the present report, these proteins and enzymes are described with the addition of unpublished results regarding their induction by peroxisome proliferators at the post-transcriptional level. Integral membrane proteins (IMPs) can be isolated using an alkaline solution of sodium carbonate. A dozen of preponderant IMPs can be seen on sodium dodecyl sulfate polyacrylamide gel electrophoresis, and the major band corresponds to a 70 kDa IMP, of which the corresponding rat **cDNA** is known. Some IMPs have been characterized by immunoblot analysis. Recently, a **cDNA** has been **cloned** for a peroxisome assembly factor (35 kDa IMP). Functions have also been proposed for some IMPs but are not yet firmly settled. Some IMPs (450/520, 70 and 26 kDa) are strongly induced by peroxisome proliferators. Our results extend to cipro- and fenofibrate the observation that the 70 kDa IMP mRNA level is strongly increased in di(2-ethylhexyl)phtalate-treated rats. All the enzyme activities associated with the peroxisomal membrane are involved in lipid metabolism: activation of substrates (fatty acids), ether lipid biosynthesis, and formation of precursors (fatty alcohols). It is believed that the same long-chain acyl-CoA synthetase occurs in the peroxisome as well as in the outer mitochondrial membrane and the endoplasmic reticulum. However, two highly homologous but different **cDNAs** encoding rat liver and brain long-chain acyl-CoA synthetases have been isolated recently. Evidence has been accumulated for a distinct synthetase that specifically activates very-long chain fatty acids. The first two steps of ether lipid biosynthesis require dihydroxyacetone-phosphate (DHAP) **acyltransferase** and alkyl-DHAP synthetase, the active sites of which are located on the inner surface of the membrane. In contrast, the catalytic site of the acyl/alkyl-DHAP reductase, which generates sn-1-alkyl-**glycerol**-3-phosphate, is located on the outer surface. Long-chain fatty alcohols, which are obligate precursors of ether lipids and wax esters, are biosynthetized by the reduction of the corresponding acyl-CoAs via the action of an acyl-CoA reductase. Peroxisome proliferators do not appear to stimulate these enzyme

activities specifically. However, we report that feno- and ciprofibrate treatments increase six-fold the palmitoyl-CoA synthetase mRNA level in the rat liver.

L29 ANSWER 42 OF 46 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 92:391418 SCISEARCH
THE GENUINE ARTICLE: JA777
TITLE: EXPRESSION OF **HUMAN** APOLIPOPROTEIN E BUT NOT THAT OF APOLIPOPROTEIN-A-I BY MOUSE C127-CELLS IS ASSOCIATED WITH INCREASED SECRETION OF LIPIDS IN THE FORM OF VESICLES AND DISKS
AUTHOR: HERSCOVITZ H (Reprint); GANTZ D; TERCYAK A M; ZANNIS V I; SMALL D M
CORPORATE SOURCE: BOSTON UNIV, HOUSMAN MED CTR, SCH MED, DEPT MED, 80 E CONCORD ST, BOSTON, MA, 02118 (Reprint); BOSTON UNIV, HOUSMAN MED CTR, SCH MED, DEPT BIOCHEM, BOSTON, MA, 02118; BOSTON UNIV, INST CARDIOVASC, DEPT BIOPHYS, BOSTON, MA, 02118; BOSTON UNIV, INST CARDIOVASC, MOLEC GENET SECT, BOSTON, MA, 02118
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF LIPID RESEARCH, (JUN 1992) Vol. 33, No. 6, pp. 791-803.
ISSN: 0022-2275.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 58
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Transfected mouse mammary-derived cells (C127) expressing **human** apolipoprotein (apo) E (C127E) were used a) to determine whether the lipid-binding character of apoE is sufficient to promote its assembly with lipid to form lipoprotein-like particles when expressed by cells not normally expressing apolipoproteins; b) to characterize the secreted complexes in terms of morphology, size, and composition; and finally c) to determine whether apoE or apoA-I **gene** expression by these transfected cells has any effect on the levels and the profiles of the synthesized and secreted lipids. The findings of the present study demonstrate that: a) as determined by density gradient ultracentrifugation and gel filtration chromatography, about 20% of the secreted [S-35]methionine-labeled apoE expressed by C127E cells is lipid-associated. b) Negative-stain electron microscopic analysis of the lipid-protein complexes recovered in the lipoprotein fractions (d < 1.21 g/ml) revealed that approximately 13% of the total population of particles were discs (16 +/- 5 nm mean diameter and 4-6 nm thick), resembling nascent high density lipoproteins (HDL). The majority of the particles however (> 82%) appeared vesicular with varying diameters (48 +/- 40 nm mean diameter). The discoidal and the vesicular appearance of the particles secreted by C127E cells is consistent with the composition of lipids. These consisted mostly of surface lipids, phospholipids (45 +/- 18%), diacylglycerols (36 +/- 17%), and free cholesterol (17 +/- 7%) (by weight). c) Expression of apoE by C127E cells was associated with an increased release of [S-35]methionine-labeled protein and [H-3] **glycerol**-labeled lipid (3- to 5- and 4- to 8-fold, respectively) compared to nontransfected C127 cells. Expression of mutant apoE or normal apoA-I, however, was not associated with increased release of the major lipid classes compared to the parent C127 cells, strongly suggesting that this character of C127E cells is specific to apoE expression. The release of lipids by C127E cells could be reduced considerably by the addition of the metabolic inhibitors, colchicine or cycloheximide (10 and 1-mu-M, respectively), suggesting that lipid release by C127E cells is an active process requiring both protein synthesis and functional secretory mechanisms. Taken together the findings suggest that apoE expression by C127 cells promotes the formation of nascent discoidal lipoprotein-like particles and enhances the release of vesicular lipids, possibly by promoting shedding of cell plasma membrane fragments.

L29 ANSWER 43 OF 46 MEDLINE on STN
ACCESSION NUMBER: 91217559 MEDLINE
DOCUMENT NUMBER: 91217559 PubMed ID: 2090719
TITLE: Perinatal hepatocyte/hepatoma hybrids: construction of **clones** that express the developmentally regulated

monoacylglycerol **acyltransferase** activity.
COMMENT: Erratum in: J Lipid Res 1991 Aug;32(8):1390
AUTHOR: Coleman R A; Bardes E S
CORPORATE SOURCE: Department of Pediatrics, Duke University Medical Center, Durham, NC 27710.
CONTRACT NUMBER: HD19068 (NICHD)
SOURCE: JOURNAL OF LIPID RESEARCH, (1990 Dec) 31 (12) 2257-64.
Journal code: 0376606. ISSN: 0022-2275.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199105
ENTRY DATE: Entered STN: 19910623
Last Updated on STN: 19970203
Entered Medline: 19910531

AB Microsomal monoacylglycerol **acyltransferase** is a developmentally expressed enzyme that catalyzes the synthesis of sn-1,2-diacylglycerol from sn-2-monoacylglycerol and palmitoyl-CoA. The activity is present in liver from fetal and suckling rats but is absent in the adult. In order to obtain a stable permanent cell line that expresses this activity, Fao rat hepatoma cells and hepatocytes from 8-day-old baby rats were hybridized and **clones** were selected. Two hybrids (HA1 and HA7) expressed monoacylglycerol **acyltransferase** activity. Like fetal hepatocytes, but unlike hepatocytes from postnatal rats, the HA cells had high rates of [14C]acetate incorporation into glycerolipids, cholesterol, and cholesteryl esters, and they secreted triacylglycerol into the media. Monoacylglycerol **acyltransferase** specific activity increased 2.5-fold as the cells divided in culture, suggesting growth-dependent regulation. The specific activities of **glycerol**-P **acyltransferase**, the committed step of the microsomal pathway of glycerolipid synthesis, and diacylglycerol **acyltransferase**, the activity unique to triacylglycerol biosynthesis, were comparable to the levels of the corresponding activities in fetal hepatocytes. Addition of insulin or dexamethasone to the media increased the incorporation of [14C]oleate into triacyglycerol about 1.7-fold within 2 h, but had little effect on [14C]oleate incorporation into phospholipid. These hormonally responsive rat-hepatoma/hepatocyte hybrids reflect the fetal stage of hepatocyte development in five major aspects of lipid metabolism: sterol, fatty acid, and triacylglycerol biosynthesis, glycerolipid secretion, and the presence of the developmentally expressed monoacylglycerol pathway.

L29 ANSWER 44 OF 46 MEDLINE on STN
ACCESSION NUMBER: 90309531 MEDLINE
DOCUMENT NUMBER: 90309531 PubMed ID: 2366629
TITLE: Modification of phospholipid polar head group with monomethylethanolamine and dimethylethanolamine decreases cholesteryl ester and triacylglycerol synthesis in cultured **human** fibroblasts.
AUTHOR: Maziere C; Auclair M; Mora L; Maziere J C
CORPORATE SOURCE: Faculte de Medecine Saint-Antoine, Paris, France.
SOURCE: LIPIDS, (1990 Jun) 25 (6) 311-5.
Journal code: 0060450. ISSN: 0024-4201.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199008
ENTRY DATE: Entered STN: 19900921
Last Updated on STN: 19980206
Entered Medline: 19900813

AB Modification of the phospholipid polar head group was achieved by supplementation of the growth medium of cultured **human** fibroblasts with the choline analogues monomethylethanolamine (ME) or dimethylethanolamine (DE) at a concentration of 80-200 micrograms/mL for 48 hr. The maximum concentration of phosphatidylmonomethylethanolamine (PME) or phosphatidyldimethylethanolamine (PDE) reached without affecting the phospholipid/protein ratio was about 45% of total phospholipids. Incorporation of oleic acid into cholesteryl esters and triacylglycerols was markedly inhibited after supplementation with ME or DE, and accounted for 60% and 40% of controls, respectively, at 200 micrograms/mL, whereas

incorporation into phospholipids was not affected. AcylCoA:cholesterol **acyltransferase** (ACAT) and diacylglycerol **acyltransferase** (DGAT) activities measured on cell-free extracts appeared to be decreased also by phospholipid polar head group modification, whereas the overall phospholipid **acyltransferase** activity remained unchanged. The intracellular content of cholesteryl esters and triacylglycerols, determined by the isotopic equilibrium method with radioactive cholesterol and **glycerol**, was found to be diminished to 50-60% and 40-50% of controls, respectively, after supplementation with the choline analogues. The study showed that modification of the phospholipid polar head group affects the activity of membrane-bound enzymes involved in the metabolism of neutral lipids.

L29 ANSWER 45 OF 46 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 88062896 EMBASE
DOCUMENT NUMBER: 1988062896
TITLE: Synthesis of a novel acetylated neutral lipid related to platelet-activating factor by acyl-CoA:1-O-alkyl-2-acetyl-sn-**glycerol acyltransferase** in HL-60 cells.
AUTHOR: Kawasaki T.; Snyder F.
CORPORATE SOURCE: Medical and Health Sciences Division, Oak Ridge Associated Universities, Oak Ridge, TN 37831, United States
SOURCE: Journal of Biological Chemistry, (1988) 263/6 (2593-2596). ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Acyl-CoA:1-O-hexadecyl-2-acetyl-sn-**glycerol acyltransferase**, a newly detected enzyme related to platelet-activating factor metabolism, has been characterized in microsomes of a **human** leukemia cell line (HL-60 cells). It has a sharp pH optimum of 6.8, does not require divalent metal ions, is stable at preincubation temperatures up to 45.degree.C, and among a variety of acyl-CoA thioesters (8:0-20:4) tested, linoleoyl-CoA is the best substrate. K(m) and V(max) values for 1-O-hexadecyl-2-acetyl-sn-**glycerol acyltransferase** are 8.5 .mu.M and 1.7 nmol/min/mg of protein, respectively. For comparative purposes acyl-CoA:1,2-dioleoyl-sn-**glycerol acyltransferase** was also characterized in HL-60 microsomes. It has a relatively broad pH optimum of 6.1, is stimulated 1.4-fold by Mg2+, is relatively labile at preincubation temperatures higher than 25.degree.C, and among the various acyl-CoA thioesters tested, myristoyl-CoA is the best substrate. In substrate competition experiments, we found 1-O-hexadecyl-2-oleoyl-sn-**glycerol** is a competitive inhibitor (K(i) = 32 .mu.M). Our findings indicate acyl-CoA:1-O-hexadecyl-2-acetyl-sn-**glycerol acyltransferase** in HL-60 cells is distinctly different from acyl-CoA:1,2-dioleoyl-sn-**glycerol acyltransferase**. Our experimental results demonstrate that the unique enzyme activity characterized in this report also is expressed in intact HL-60 cells.

L29 ANSWER 46 OF 46 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1981:158333 BIOSIS
DOCUMENT NUMBER: PREV198171028325; BA71:28325
TITLE: EVIDENCE FOR STIMULATION OF GLYCERO PHOSPHO LIPID SYNTHESIS IN CULTURED **HUMAN** CELLS INFECTED WITH MEASLES VIRUS.
AUTHOR(S): SUZUKI Y [Reprint author]; MOCHIZUKI T; MATSUMOTO M
CORPORATE SOURCE: DEP BIOCHEM, SHIZUOKA COLL PHARM, SHIZUOKA, SHIZUOKA 422
SOURCE: Journal of Biochemistry (Tokyo), (1980) Vol. 88, No. 2, pp. 539-546.
CODEN: JOBIAO. ISSN: 0021-924X.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
AB Change of lipid metabolism in FL cells derived from **human** amniotic membrane during fusion from within induced by measles virus was studied. The following results were obtained. Incorporation of

[32P]orthophosphate and [methyl-14C]choline into the lipid fraction of infected cells was higher than that of control cells. In this case, no detectable alteration of labeled phospholipid composition was observed. Radioactivity of the lipids in subcellular fractions of infected-cells labeled with [1-14C]oleic acid for a short term also increased. Specific enzyme activities in phosphatidylcholine synthesis, i.e., ATP: choline phosphotransferase [EC 2.7.1.32], CTP: phosphocholine cytidyltranferase [EC 2.7.7.15], and CDP choline: 1,2-diacylglycerol cholinephosphotransferase [EC 2.7.8.2] in each subcellular fraction of the infected-cells were higher than those of control cells. AcylCoA: 1-acyl-GPC [sn-glycero-3-phosphocholine] **acyltransferase** activity in microsomal fraction of the infected cells was enhanced. The above results indicate that there is stimulation of cellular phospholipid synthesis in de novo pathway and acylation of lysophospholipids in the infected cells. A marked increase in radioactivity-incorporation (10.3 fold) of [1-14C]oleic acid into triacylglycerol in the cytosol of the infected cells was also observed.

=> log y